American Journal of Industrial Medicine 20:219–227 (1991)

Testicular Cancer in Young Men and Parental Occupational Exposure

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To investigate whether parental occupation, especially during the 12 month period before birth, could be responsible for elevated rates of testicular cancer in young men, we used data from a case-control study of 223 cases and 212 controls conducted in the Washington, DC area. For all histologic types of testicular cancer combined, no significant associations were found for specific occupations, nor for the broad occupational categories of professional, other white collar, or blue collar workers. However, for cases with seminomas, excess risks were seen for those with parents employed in the following occupations: mothers in health-related occupations, O.R. = 4.6 (1.1–19.1), and fathers working in automobile service stations, O.R. = 4.0 (0.6–24.5), manufacturing industries, O.R. = 2.2 (1.0–4.2), and aircraft production and maintenance, O.R. = 5.3 (0.7–24.1), Although these findings for seminoma are intriguing, they do not explain the increase of testicular cancer in young men.

Key words: seminoma, germinal tumors, prenatal exposure

INTRODUCTION

Over the past forty years, the incidence of testicular cancer in the United States has been increasing dramatically for young adult men, aged 15–44 years. The highest rates are seen for men in the age group 25–34 years [Brown et al., 1986b]. Because of this unusual young adult peak, it has been speculated that pre- and perinatal factors may play a role in the etiology of testicular cancer [Brown et al., 1986a; Depue et al., 1983; Moss et al., 1986]. Although in-utero exposures (e.g., parental exposure to sedatives or x-rays), abnormal uterine bleeding, low birth weight, and cryptorchidism have been associated with testicular cancer, the increases in risk were not great enough to explain the rise in incidence among young men [Brown et al., 1986a; Brown et al., 1987]. To uncover other factors that could have influenced the development of testicular cancer early in life, we used data from a case-control study conducted in the Washington D.C. area. This is the first investigation of the etiologic role of parental occupation, including exposures in-utero, in the development of testicular cancer.

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Accepted for publication November 15, 1990.

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POPULATION AND METHODS

Cases for this study consisted of all living cases (308) of testicular cancer, aged 18–42 years, newly diagnosed between January 1976 and July 1981, and referred to one of three participating hospitals. Controls (288) were selected from other male cancer patients, excluding genital tract cancer, at the same hospitals. Cases and controls were similar in age (within 2 years) and time period of diagnosis. The participating hospitals were the National Institutes of Health Clinical Center, the Bethesda Naval Hospital, and the Walter Reed Army Medical Center, all located in the Washington, DC area [Pottern et al., 1985].

Interviews, which included information on the father's usual occupation during the childhood of the subject, were conducted with 271 (88%) cases and 259 (90%) controls. In-person interviews were conducted in the hospital for the cases and controls who were seen on the wards during 1979–81, while telephone interviews were conducted with cases and controls diagnosed prior to 1979.

In addition to the interviews of the cases and controls, telephone interviews were conducted with their biological mothers during 1979–1981. The mothers of 225 cases (84%) and 212 controls (82%) were successfully interviewed, using a standardized questionnaire administered by trained interviewers [Brown et al., 1986a]. The occupational portion of the interview included detailed job histories (including volunteer work and vocational or college training, but excluding activities as a housewife) of both the father and the mother during the year before birth (prenatal period). Information was collected for the months during the prenatal period that each job was held, and included job and industry titles. Each position with a particular set of duties or job title was considered as a separate job. The parental occupations were coded according to the Standard Occupational Classification (1977) and the Standard Industrial Classification (1972), without knowledge of the case or control status of the sons. The materials handled were grouped using a coding scheme developed for this study by one of the authors (LMP).

Pathology reports were used to determine the histological type of the testicular tumors. Non-germinal tumors, one case with a Leydig cell tumor, and one case with a yolk sac tumor, were excluded from the present analysis. Risks were calculated for germinal cell tumors ($n = 223$) and separately for a major histological subgroup, the seminomas ($n = 42$).

The association between occupational exposure and testicular cancer was measured by the Odds Ratio (O.R.), as an approximation of the relative risk, applying a 95% confidence interval (C.I.), using exact calculations according to Thomas [1975]. For each specific occupation, the unexposed group was defined as "all other occupations." This implies that subjects may be considered as exposed in some analyses and unexposed in others.

RESULTS

As shown in Table I, almost all of the fathers of study subjects were employed during the one year prenatal period. About one-third of the mothers had employment other than as a housewife during this one year period. There was no significant difference between the cases and controls in the distribution of the number of reported jobs of the parents. Eighty-four percent of the fathers held the same job during the

TABLE I. Distribution of Jobs Held During the Prenatal Period Among the Parents of Testicular Cancer Cases and Controls*

Number of jobs held	Cases No. = 223				Controls No. = 212			
	Father		Mother		Father		Mother	
0	4	2%	161	72%	3	1%	142	67%
1	176	79%	55	25%	175	83%	66	31%
2	36	16%	6	3%	26	12%	4	2%
3	5	2%	1	0%	7	3%	—	
4	2	1%	—		—		—	
5	0		—		1	0%	—	

*The prenatal period is the one-year period before birth of the study subject.

entire prenatal year. Only 5% of all fathers had a different job in the 3 months before conception than during the pregnancy. Of the employed mothers, 31% held a job during all of the pregnancy and 52% during the first 2 trimesters of pregnancy. There was no relationship between disease risk and the age of the parents at their sons' birth (chi square testing for homogeneity of cases and controls over the age-quartiles resulted in $p = 0.69$ for all testicular tumors and 0.26 for seminomas with respect to father's age, and $p = 0.80$ and 0.89 respectively for mother's age). Consequently, we present odds ratios unadjusted for parental age.

Parental Employment by Industry

Table II shows the risk for testicular cancer associated with employment in major categories of industry for each parent during the one year prenatal period. No significantly elevated risks were noted for father's employment. While one of the confidence intervals for the mothers did not contain 1.0, it was based on only 3 cases. For the father's usual industry of employment during the childhood of the son, the only noteworthy risk was for seminoma associated with the manufacturing industry (O.R. = 2.2 (1.0–4.2), 14 cases, 39 controls). When more specific industrial categories were examined, none of the risks were significantly elevated.

Parental Employment by Occupation

Associations for the usual occupation of the father during childhood of the subject and the occupations of the father and the mother during the prenatal period are presented for all testicular tumors in Table III and for seminoma in Table IV. Employment by the father during the prenatal period as a professional, other white collar worker, or blue collar worker was not associated with a significant increase in testicular cancer risk, either for all germinal cell cancer (Table III) or for seminoma (Table IV). Examination of occupational groups within these broad categories revealed no statistically significant associations with testicular cancer among the sons. Non-significant elevations in testicular cancer risk of the sons were found for all germinal cell tumors among repairers of electrical and electronic equipment, and for seminoma among those employed in health-related occupations. Sons of mechanics and machinery repairers (including service station workers) had a marginally significant excess risk for seminoma (O.R. = 2.6).

Findings for usual occupation of the father during the subjects' childhood were

TABLE II. Risks for All Testicular Tumors Associated With Parental Employment in Major Industrial Categories During the Subject's Prenatal Period*

	Father				Mother			
Industry	Ca[a]	Co[b]	O.R.	C.I.	Ca[a]	Co[b]	O.R.	C.I.
Agriculture, forestry, fishing	16	21	0.7	0.3 – 1.5	2	0	∞	0.3 – ∞
Mining	3	9	0.3	0.1 – 1.3	—	—		
Construction	17	21	0.8	0.4 – 1.5	1	0	∞	0.1 – ∞
Manufacturing	59	58	1.0	0.6 – 1.5	16	21	0.7	0.4 – 1.4
Transportation, communication, others	31	25	1.2	0.7 – 2.2	3	0	∞	5.6 – ∞
Wholesale trade	9	16	0.6	0.2 – 1.4	0	2	0.0	0.0 – 3.3
Retail trade	29	19	1.5	0.8 – 3.0	14	15	0.9	0.4 – 2.0
Finance, insurance, real estate	4	6	0.6	0.1 – 2.7	2	5	0.4	0.0 – 2.3
Services	30	31	0.9	0.5 – 1.6	26	21	1.2	0.6 – 2.3

*The prenatal period is the one-year period before birth of the study subject. The total number of cases is 223; the total number of controls is 212.
[a]Ca = number of employed cases.
[b]Co = number of employed controls.

generally similar to those for employment during the prenatal period. Although based on small numbers, non-significantly elevated risks for germinal cell tumors and for seminoma were seen for paternal employment in health-related occupations. There was also a non-significant association for seminoma with usual occupation as a mechanic or machinery repairer, O.R. = 3.4.

No association was found for employment compared to non-employment of the mother during the prenatal period, for all testicular cancer, O.R. = 0.8 (0.5–1.2) or for seminoma, O.R. = 0.9 (0.4–1.9). Similar to the findings for the fathers, no significant excess risk was found associated with the mother's occupation during the prenatal period in the broad categories of professional, other white collar, or blue collar occupations. Among specific occupational groups, a significantly elevated association for seminoma was found for mothers employed in health-related occupations, O.R. = 4.6 (1.1–19.1).

Medical and Health-Related Occupations

When data were combined for all employment in the medical field (i.e. health related occupations, physicians, and all persons with an industry classification for hospitals), a non-significant excess risk for seminoma was found, associated with prenatal paternal employment, O.R. = 1.7 (0.2–10.0). No single occupation was dominant (3 nurses, 2 physicians, 1 chiropractor, 1 radiology technician, 1 lab technician, and 3 non-specific hospital workers). The risk associated with maternal employment in the medical field, O.R. = 4.6, was largely due to a significantly elevated risk for the sons of mothers employed as nurses during the prenatal period, O.R. = 5.5 (1.5–15.9).

Because of our previous findings in this study group [Brown et al., 1986a], of an association of in utero diagnostic x-ray exposure with all testicular tumors, O.R. = 2.3 (1.2–4.6) and with seminoma, O.R. = 3.3 (1.3–8.8), we examined whether the findings of increased risk for testicular cancer among the sons of the medical workers might be partly due to prenatal occupational exposure to x-rays. For nine fathers and four mothers, there was a self-reported occupational exposure to x-rays.

TABLE III. Risks for Germinal Tumors Associated With Paternal Usual Occupation During Subject's Childhood and With Employment of the Father and the Mother During the Subject's Prenatal Period*

	Father								Mother			
	Usual				Prenatal Period				Prenatal Period			
Occupation	Ca[a]	Co[b]	O.R.	C.I.	Ca[a]	Co[b]	O.R.	C.I.	Ca[a]	Co[b]	O.R.	C.I.
Professionals	50	45	1.1	0.7–1.7	34	32	1.0	0.6–1.8	5	11	0.4	0.1–1.3
Administrators	18	21	0.8	0.4–1.6	13	8	1.6	0.6–4.5	1	1	1.0	0.0–75.0
Teachers	4	5	0.8	0.1–3.6	5	8	0.6	0.1–2.1	1	7	0.1	0.0–1.0
Physicians, veterinarians	3	3	1.0	0.1–7.2	0	2	0.0	0.0– ∞	—	—		
Other professionals	25	16	1.5	0.8–3.2	17	15	1.1	0.5–2.4	3	3	1.0	0.1–7.2
Other white-collar workers	52	41	1.3	0.8–2.1	58	52	1.1	0.7–1.7	49	42	1.1	0.7–1.9
Health-related	4	1	3.9	0.4–190.7	3	2	1.4	0.2–17.3	9	6	1.4	0.4–5.0
Engineers, scientists	3	5	0.6	0.1–2.9	5	3	1.6	0.3–10.4	1	0	∞	0.1– ∞
Other technicians	3	2	1.4	0.2–17.3	1	2	0.5	0.0–9.2	0	1	0.0	0.0–18.1
Sales, personal services	35	29	1.2	0.7–2.0	38	31	1.2	0.7 2.0	13	14	0.9	0.4–2.0
Clerks	7	4	1.7	0.4–8.0	12	16	0.7	0.3–1.6	27	21	1.3	0.7–2.4
Blue-collar workers	116	119	0.9	0.6–1.3	139	136	0.9	0.6–1.4	11	19	0.5	0.3–1.2
Agriculture, forestry	8	19	0.4	0.1–0.9[c]	19	20	0.9	0.4–1.8	1	0	∞	0.1– ∞
Construction trades	23	26	0.8	0.4–1.6	16	31	0.5	0.2–0.9[c]	—	—		
Mining	4	4	0.9	0.2–5.2	1	3	0.3	0.0–4.0	—	—		
Transportation, communication, etc.	23	15	1.5	0.7–3.2	26	21	1.2	0.6–2.3	—	—		
Mechanics, machinery repair	8	8	0.9	0.3–3.0	13	17	0.7	0.3–1.6	—	—		
Electrical, electronics repair	3	2	1.4	0.2–17.3	6	2	2.9	0.5–29.7	—	—		
Other repairers	3	4	0.7	0.1–4.2	3	3	1.0	0.1–7.2	—	—		
Production workers	30	24	1.2	0.7–2.3	42	39	1.0	0.6–1.7	7	14	0.5	0.2–1.2
Manual occupations	2	3	0.6	0.1–5.6	9	8	1.1	0.4–3.3	0	3	0.0	0.0–1.6

*The prenatal period is the one-year period before the birth of the study subject. The total number of cases is 223; the total number of controls is 212.

[a]Ca = number of employed cases.

[b]Co = number of employed controls.

[c]Marks an O.R. for which the 95% C.I. does not contain unity.

TABLE IV. Risks for Seminoma Associated With Paternal Usual Occupation During Subject's Childhood and With Parental Employment During the Subject's Prenatal Period*

	Father								Mother			
	Usual				Prenatal Period				Prenatal Period			
Occupation	Ca[a]	Co[b]	O.R.	C.I.	Ca[a]	Co[b]	O.R.	C.I.	Ca[a]	Co[b]	O.R.	C.I.
Professionals	8	45	0.9	0.3–2.1	5	32	0.8	0.2–2.2	2	11	0.9	0.1–4.4
Administrators	2	21	0.5	0.0–2.0	1	8	0.6	0.0–4.9	0	1	0.0	0.0–95.9
Teachers	1	5	1.0	0.0–9.4	1	8	0.6	0.0–4.9	0	7	0.0	0.0–2.7
Physicians, veterinarians	1	3	1.7	0.0–21.7	0	2	0.0	0.0–17.6	—	—		
Other professionals	4	16	1.3	0.3–4.3	3	15	1.0	0.2–3.8	2	3	3.4	0.3–31.2
Other white-collar workers	10	41	1.3	0.5–3.0	13	52	1.4	0.6–3.0	11	42	1.4	0.6–3.2
Health-related	1	1	5.1	0.1–405.8	2	2	5.2	0.4–73.6	5	6	4.6	1.1–19.1[c]
Engineers, scientists	0	5	0.0	0.0–4.2	0	3	0.0	0.0–8.7	—	—		
Other technicians	0	2	0.0	0.0–17.6	0	2	0.0	0.0–17.6	0	1	0.0	0.0–95.9
Sales, personal services	7	29	1.3	0.4–3.3	9	31	1.6	0.6–3.8	2	14	0.7	0.1–3.3
Clerks	2	4	2.6	0.2–18.8	2	16	0.6	0.1–2.8	4	21	1.0	0.2–3.1
Blue-collar workers	23	119	0.9	0.5–2.0	24	136	0.7	0.4–1.6	1	19	0.2	0.0–1.7
Agriculture, forestry	0	19	0.0	0.0–0.8[c]	3	20	0.7	0.1–2.7	—	—		
Construction trades	4	26	0.8	0.2–2.4	2	31	0.3	0.0–1.2	—	—		
Mining	1	4	1.3	0.0–13.2	0	3	0.0	0.0–8.7	—	—		
Transportion, communication, etc.	5	15	1.8	0.5–5.5	2	21	0.5	0.0–2.0	—	—		
Mechanics, machinery repair	5	8	3.4	0.8–12.6	8	17	2.6	0.9–7.2	—	—		
Electrical, electronics repair	0	2	0.0	0.0–17.6	1	2	2.5	0.0–50.0	—	—		
Other repairers	0	4	0.0	0.0–5.7	0	3	0.0	0.0–8.7	—	—		
Production workers	6	24	1.3	0.4–3.6	7	39	0.9	0.1–2.2	0	14	0.0	0.0–1.2
Manual occupations	0	3	0.0	0.0–8.7	2	8	1.3	0.3–6.7	0	3	0.0	0.0–8.7

*The prenatal period is the one-year period before the birth of the study subject. The total number of cases is 42; the total number of controls is 212.

[a]Ca = number of employed cases.

[b]Co = number of employed controls.

[c]Marks an O.R. for which the 95% C.I. does not contain unity.

For the maternal occupations with x-ray exposure, there was no excess risk for either germinal tumors or seminomas. A significantly increased risk for seminoma was found associated with paternal occupational exposure to x-rays, O.R. = 5.4 (1.0–30.4). When the mother's exposure to diagnostic x-rays during pregnancy was considered as a potential confounder, the risk for seminomas associated with maternal employment in the medical field remained elevated O.R. = 3.3 (1.2–8.8). All four mothers with reported occupational exposure to x-rays were nurses. No assessment of the separate association of maternal occupation and of occupational x-ray exposure with testicular cancer risk was possible.

When occupational x-ray exposure was considered as a confounder, the 1.7-fold risk for seminomas associated with paternal employment in the medical field was reduced, O.R. = 0.7 (0.0–5.1). If the employment in the medical field was considered as a potential confounder, the risk associated with paternal occupational x-ray exposure remained elevated, O.R. = 7.2 (0.9–87.8).

Hydrocarbon-Related Occupations

For pre-natal parental employment in occupations with potential exposure to hydrocarbons, no excess risk was noted for all testicular tumors, O.R. = 1.1 (0.6–2.1), or for seminomas, O.R. = 1.2 (0.3–3.4). Hydrocarbon-related occupations included car or aircraft mechanics, engine repairers, machinists, light truck drivers, gas and service station attendants, painters, and printers. Of these various subgroups, an elevated risk was found only for seminomas among sons of service station workers, O.R. = 4.0 (0.6–24.5), based upon three cases and four controls.

DISCUSSION

This is the first case-control study of testicular cancer to investigate the role of in utero and childhood exposures related to parental occupation. To accomplish this, we obtained the father's usual occupation from the interview with the study subject and by direct interview with the subject's mother, obtained a complete job history for the one-year prior to birth for both parents. This approach provides superior information to that from limited data sources such as birth certificates.

Perhaps the most intriguing finding in our study was an association of seminoma risk with prenatal parental employment in the medical field. The association was present for both mothers' and fathers' employment. For fathers, this association was not specific to any one occupation and was based upon small numbers. For mothers, the association was largely due to the excess risk among sons of nurses. No such association was found for the sons of professional or other white collar workers as a group.

Workers in the medical field may have some potentially hazardous exposures. Both exposed women and wives of men exposed to waste anesthetic gases have been reported to have more spontaneous abortions and congenital anomalies than expected [Cohen et al., 1974; 1975]. Occupational x-ray exposure may also occur in many of these occupations. For the mothers in our study who had reported prenatal occupational x-ray exposures, no risk of testicular cancer was evident among their sons. In this study, diagnostic x-ray exposure of the mothers during pregnancy was associated with testicular cancer risk [Brown et al., 1968a] and was far more prevalent (16% of the case mothers) than was occupational x-ray exposure (1% of the case mothers).

Mother's diagnostic x-ray exposure did not explain the excess risk for seminomas among sons of mothers in the medical field. There was a large significant excess risk for seminoma associated with father's prenatal occupational x-ray exposure (OR = 5.4). The nonsignificant excess risk associated with father's employment in the medical field (OR = 1.7) may actually be due to prenatal paternal occupational exposure to x-rays.

No excess risk for testicular cancer was found associated with prenatal parental hydrocarbon-related occupations as a group. However, a nonsignificant excess risk (OR = 4.0) was found for sons of fathers who had worked in service stations. For cancers at other sites, parental occupations involving exposure to hydrocarbons have been implicated, although the overall results show no consistent association [I.A.R.C., 1989; Arundel and Kinnier-Wilson, 1986]. Nonsignificant increases in testicular cancer among sons of fathers employed in the aircraft production and maintenance industry were also seen. Although exposure to dimethylformamide has been linked to the risk of testicular cancer in aircraft maintenance workers [Ducatman, 1986], it is not known whether this chemical could be responsible for the increased risk of testicular cancer in the offspring of aircraft workers in our study.

A potential source of bias in case-control studies such as this one is differential recall for cases and controls [Sackett, 1979]. Mothers of severely ill offspring are more likely to recall events of the pregnancy of that child than are mothers of healthy children [Kwa et al., 1980]. To eliminate this bias, and to minimize differences in selection due to referral patterns, we purposely chose as our comparison population subjects with other types of malignancies. It is possible that positive associations in our study could have been missed if other cancers in our control group shared common risk factors related to parental occupation. However, no substantial differences in the risks were seen when hematopoietic cancers (cancers previously associated with parental occupations) were excluded from the analysis.

This study did not find substantial risks for testicular tumors associated with prenatal parental occupational exposure. Suggestive findings included elevated risks of seminoma with maternal employment in the medical field, paternal exposure to occupational x-rays, and paternal employment in service stations, manufacturing, and the aircraft industry.

ACKNOWLEDGMENTS

The authors thank Dr. Nasa Javadpour, Division of Cancer Treatment, NCI, Dr. Kevin J O'Connell, Bethesda Naval Hospital, and Dr. Ray E Stutzman, Walter Reed Army Medical Center, for their contributions in the data collection; Dr. Jerry LR Chandler, National Cancer Institute, for helpful advice; Ms. Jeanne Rosenthal, Ms. Kathy Weber, Ms. Judith Walsh, Ms. Sandra Becker, and the staff of Westat Inc. for data management and interviewing; and Ms. Roselyn Weil, NCI, for data collection and interviewing.

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